

What is claimed is:

1. A method of inhibiting CD1-mediated inflammation, comprising contacting a CD1-expressing cell with an inhibitor of microsomal triglyceride transfer protein (MTP), wherein activation of a CD1-restricted T cell is reduced following contact of said CD1-expressing cell with an inhibitor of MTP.

2. The method of claim 1, wherein said CD1-expressing cell is an antigen presenting cell.

3. The method of claim 2, wherein said antigen presenting cell is selected from the group consisting of a B cell, a monocyte, a macrophage, a dendritic cell, a hepatocyte, and an epithelial cell.

4. The method of claim 1, wherein said CD1-expressing cell is an epithelial cell.

5. The method of claim 1, wherein said CD1-expressing cell is an intestinal epithelial cell.

6. The method of claim 1, wherein said CD1-expressing cell is a CD1-d expressing cell.

7. The method of claim 6, wherein said CD1-d expressing cell expresses a natural killer receptor or an invariant T cell receptor.

8. The method of claim 7, wherein said invariant T cell receptor comprises human V α 24J α 15.

9. A method of inhibiting CD1-mediated antigen presentation, comprising contacting a CD1-expressing cell with an inhibitor of microsomal triglyceride transfer protein (MTP), wherein the amount of lipid associated with CD1 or the amount of binding of MTP to CD1 is reduced in the presence of said inhibitor compared to the amount in the absence of said inhibitor.

10. A method of inhibiting a symptom of a CD1-mediated immunopathology, comprising administering to a mammal a MTP inhibitor, wherein said symptom is reduced following administration.

11. The method of claim 10, wherein said immunopathology is an autoimmune disorder.

12. The method of claim 10, wherein said immunopathology is selected from the group consisting of colitis or hepatitis.

13. A method of inhibiting an association of MTP and CD1, comprising contacting a cell expressing said MTP and said CD1 with an MTP-binding compound, wherein said association is reduced in the presence of said compound compared to that in the absence of said compound.

14. A method of inhibiting an association of MTP and CD1, comprising contacting a cell expressing said MTP and said CD1d with an CD1-binding compound, wherein said association is reduced in the presence of said compound compared to that in the absence of said compound.

15. A method of reducing lipidation of CD1d in a cell, comprising contacting said cell with, a compound which inhibits binding of a alpha 1, alpha 2, or alpha 3 domain of CD1d with MTP.

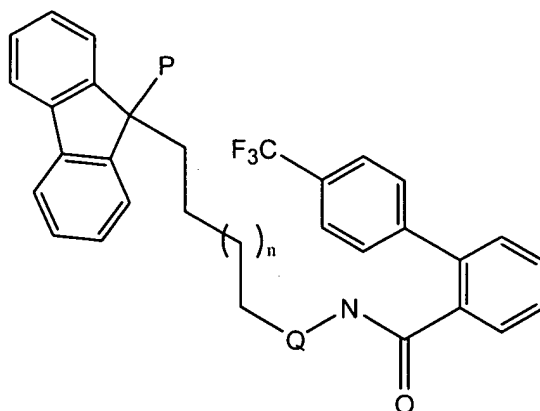
16. A method inhibiting inflammation, comprising administering to an inflamed tissue a microsomal triglyceride transfer protein (MTP) inhibitor.

17. The method of claim 16, wherein said tissue is intestinal epithelial tissue.

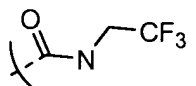
18. The method of claim 16, wherein said inflammation is skeletal inflammation, gastrointestinal inflammation, cardiovascular inflammation, pulmonary inflammation, or neurological inflammation.

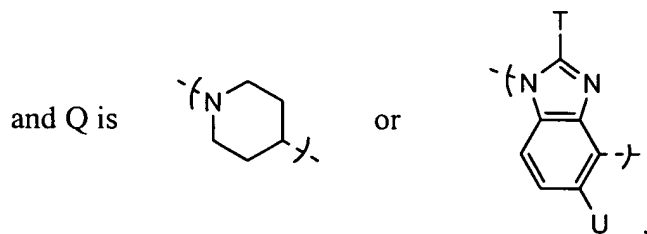
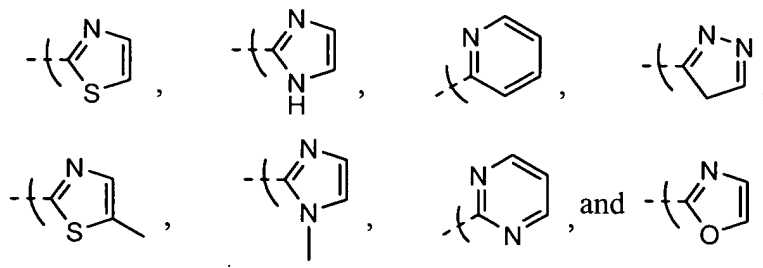
19. The method of claim 18, wherein said gastrointestinal inflammation is colitis.

20. The method of claim 16, wherein said tissue is pulmonary tissue, liver tissue, intestinal tissue or dermal tissue.
21. The method of claim 16, wherein said MTP inhibitor is a compound according to Formula I:
- I.



wherein n is zero or 1;

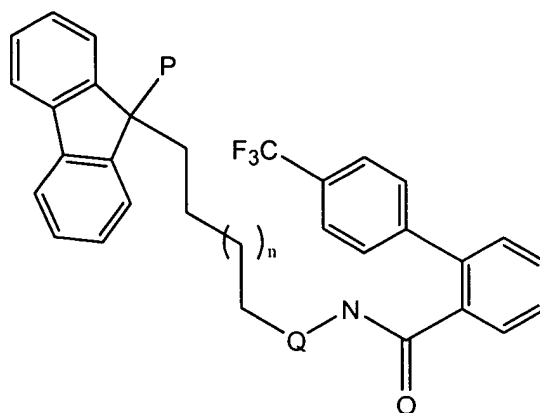
P is  or a 5- or 6- membered heterocycle selected from the group consisting of:



wherein T and U are, independently, hydrogen or lower alkyl.

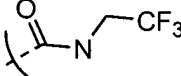
22. The method of claim 16, wherein said MTP inhibitor is a compound according to Formula I:

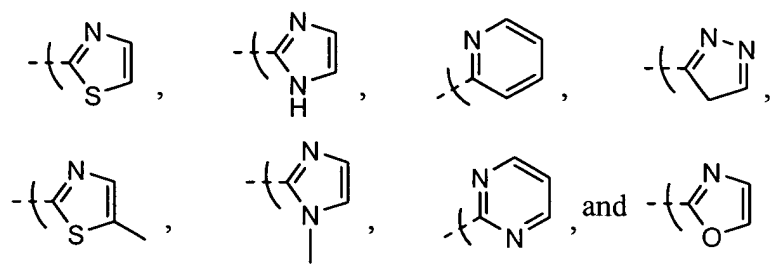
I.



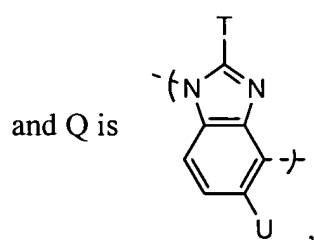
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wherein n is zero or 1;

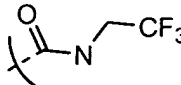
P is  or a 5- or 6- membered heterocycle selected from the group consisting of:



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wherein T and U are, independently, hydrogen or lower alkyl.

23. The method of claim 22, wherein P is .

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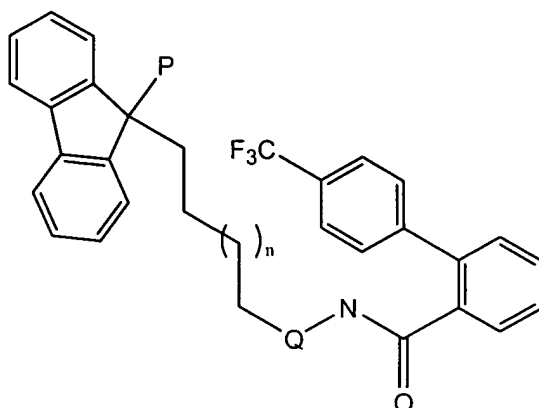
24. The method of claim 16, wherein said MTP inhibitor is a MTP antisense nucleic acid or a MTP siRNA.

25. The method of claim 24, wherein the siRNA comprises the nucleic acid sequence of SEQ ID NO:1 or SEQ ID NO:2.

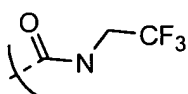
26. A method of preventing or alleviating a symptom of an inflammatory disorder comprising identifying a subject suffering from or at risk of developing said inflammatory disorder and administering to said subject a microsomal triglyceride transfer protein (MTP) inhibitor.

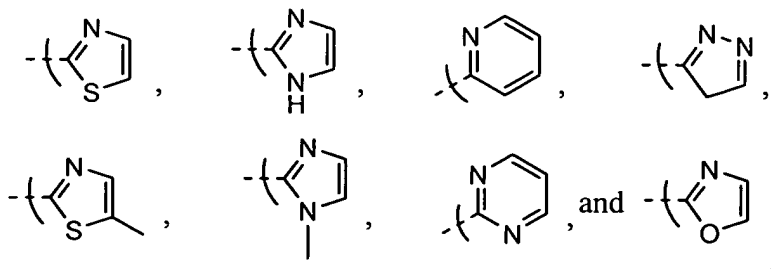
27. The method of claim 26, wherein said MTP inhibitor is a compound according to Formula I:

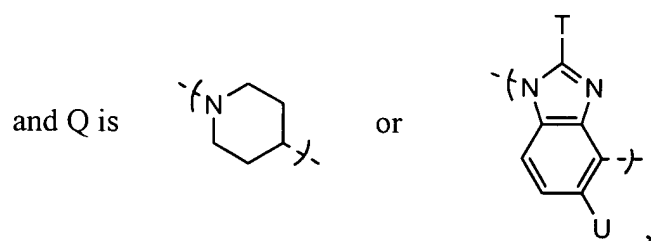
I.



wherein n is zero or 1;

P is  or a 5- or 6- membered heterocycle selected from the group consisting of:

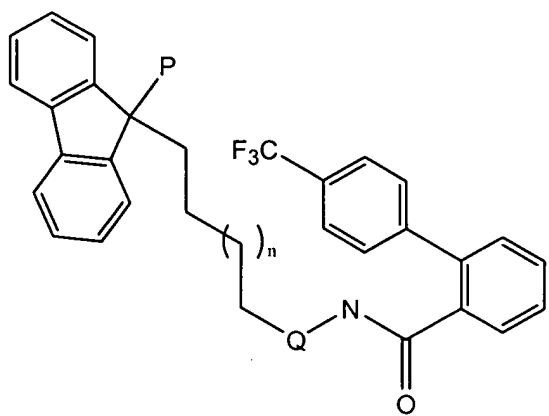




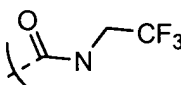
wherein T and U are, independently, hydrogen or lower alkyl.

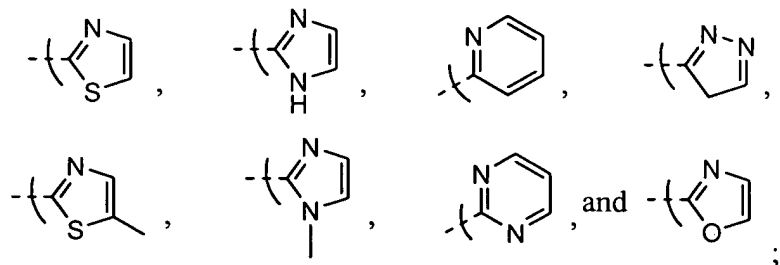
- 5 28. The method of claim 26, wherein said MTP inhibitor is a compound according to Formula I:

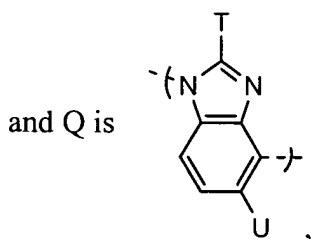
I.



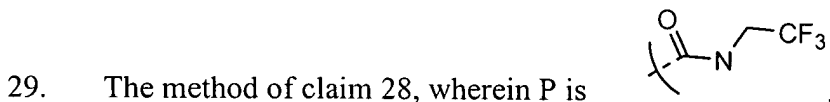
10 wherein n is zero or 1;

P is  or a 5- or 6- membered heterocycle selected from the group consisting of:





wherein T and U are, independently, hydrogen or lower alkyl.



30. The method of claim 26, wherein said MTP inhibitor is a MTP antisense nucleic acid or MTP siRNA.

31. The method of claim 26, wherein the siRNA comprises the nucleic acid sequence of SEQ ID NO:1 or SEQ ID NO:2.

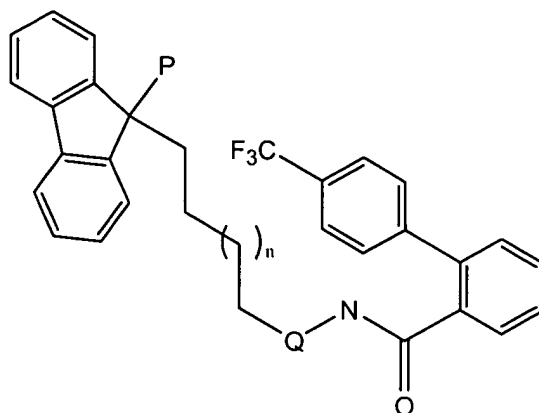
32. The method of claim 26, wherein said inflammatory disorder is a skeletal inflammatory disorder, a gastrointestinal inflammatory disorder, an oral inflammatory disorder, a cardiovascular inflammatory disorder, a pulmonary inflammatory disorder, an auto-immune disorder or a neurological inflammatory disorder.

33. The method of claim 32, wherein said gastrointestinal disorder is inflammatory bowel disease, Crohn's disease or colitis.

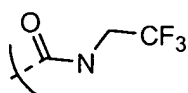
34. A method of inhibiting tissue inflammation comprising contacting a cell with a MTP inhibitor in an amount that inhibits the production of an inflammatory cytokine.

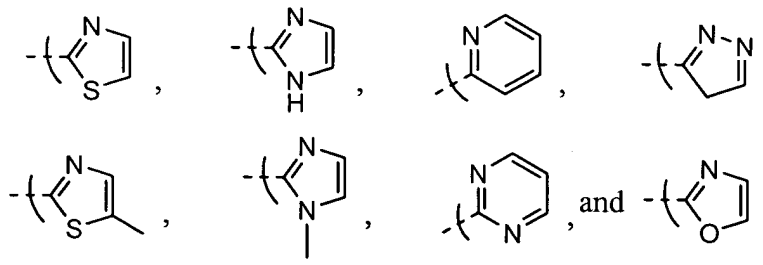
35. The method of claim 34, wherein said MTP inhibitor is a compound according to Formula I:

I.

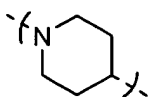


wherein n is zero or 1;

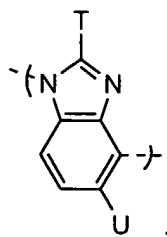
P is  or a 5- or 6- membered heterocycle selected from the group consisting of:



and Q is

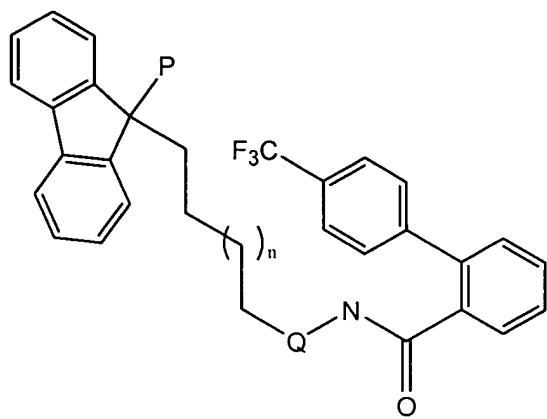


or

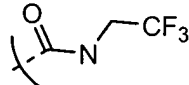


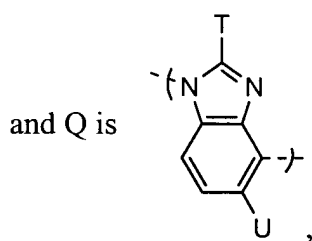
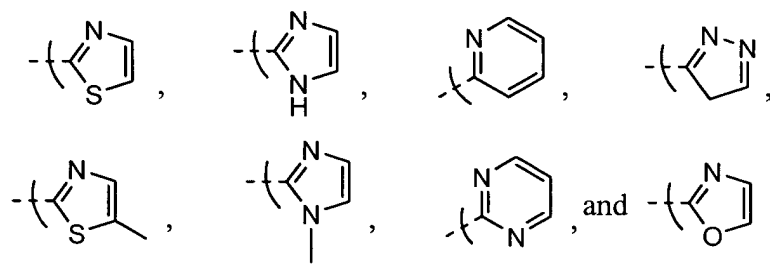
wherein T and U are, independently, hydrogen or lower alkyl.

36. The method of claim 34, wherein said MTP inhibitor is a compound according to Formula I:
I.



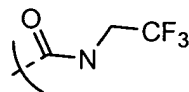
wherein n is zero or 1;

P is  or a 5- or 6- membered heterocycle selected from the group consisting of:



wherein T and U are, independently, hydrogen or lower alkyl.

37. The method of claim 34, wherein P is



38. The method of claim 34, wherein said MTP inhibitor is a MTP antisense nucleic acid or a MTP siRNA.

39. The method of claim 38, wherein the siRNA comprises the nucleic acid sequence of SEQ ID NO:1 or SEQ ID NO:2.

40. The method of claim 34, wherein said cell is a hepatocyte or an epithelial cell.

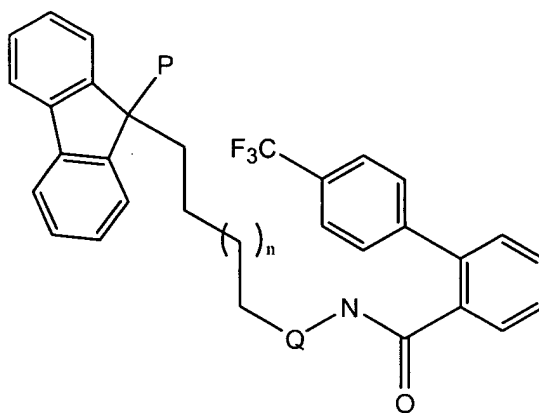
41. The method of claim 40, wherein said epithelial cell is an intestinal epithelial cell.

42. The method of claim 34, wherein said inflammatory cytokine is interferon, interleukin or tumor necrosis factor alpha.

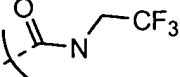
43. A method of inhibiting tissue inflammation, comprising contacting a cell with a MTP inhibitor in an amount that inhibits T-cell activation.

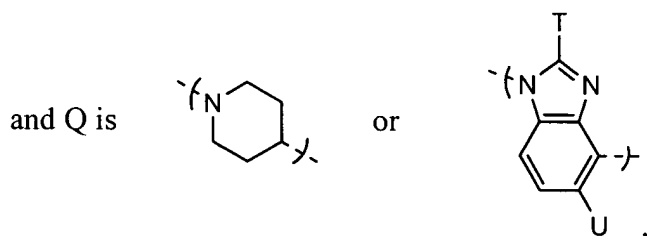
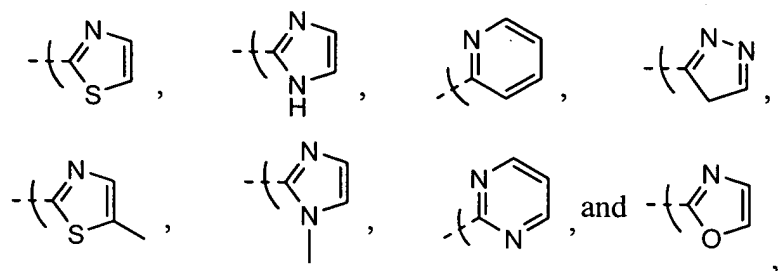
44. The method of claim 43, wherein said MTP inhibitor is a compound according to Formula I:

I.



wherein n is zero or 1;

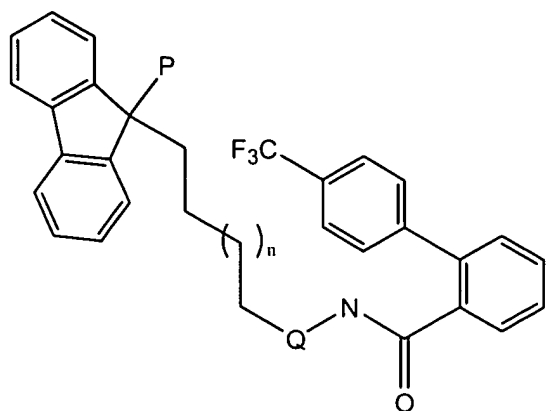
P is  or a 5- or 6- membered heterocycle selected from the group consisting of:



wherein T and U are, independently, hydrogen or lower alkyl.

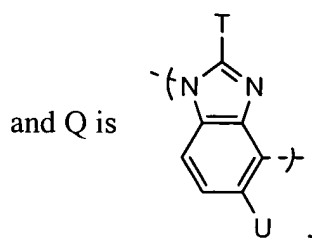
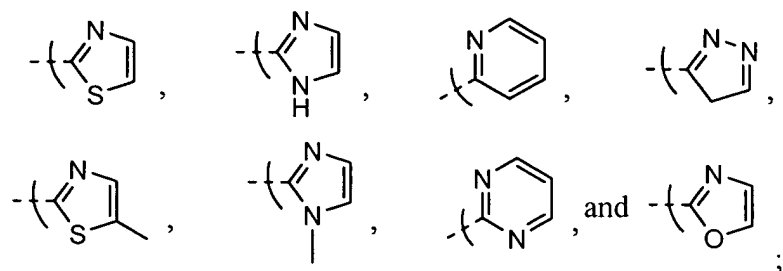
45. The method of claim 43, wherein said MTP inhibitor is a compound according to Formula I:

I.



wherein n is zero or 1;

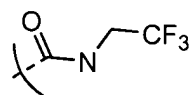
P is $-(\text{N}(\text{CF}_3)\text{CH}_2\text{C}(=\text{O}))-$ or a 5- or 6- membered heterocycle selected from the group consisting of:



wherein T and U are, independently, hydrogen or lower alkyl.

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46. The method of claim 44, wherein P is



47. The method of claim 43, wherein said MTP inhibitor is a MTP antisense nucleic acid or MTP siRNA.

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48. The method of claim 47, wherein the siRNA comprises the nucleic acid sequence of SEQ ID NO:1 or SEQ ID NO:2.

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49. The method of claim 43, wherein said cell is a hepatocyte or an epithelial cell.

50. The method of claim 49, wherein said epithelial cell is an intestinal epithelial cell.